SACHRP Recommendation on Consideration of Local Context With Respect to Increasing Use of Single IRB Review

SACHRP recognizes that there is more use of single IRBs for review for multi-site studies and single site studies that are reviewed by an IRB external to the site where the research is conducted. Even so, institutions are still often reluctant to cede authority for IRB review and those IRBs that review regularly at sites external to them, i.e., independent IRBs and central IRBs, have developed additional procedures to address local context that are burdensome and rarely provide information useful to reviewing the research. These concerns apply to all types of research, not just clinical research. For example, it applies to social behavioral research such as in the fields of anthropology and social work and other areas such as epidemiological research. It is believed that the current practices are in part the consequence of guidance from OHRP and FDA.

SACHRP commends OHRP for the actions it has taken recently to clarify the Office's view regarding local context. OHRP has archived its 1998 guidance on Knowledge of Local Context, and has issued a letter dated April 30, 2010, which clarifies that OHRP fully agrees with the Food and Drug Administration's position on the benefits of relying on a single central IRB for multicenter research. OHRP also addressed the issue of non-local IRB review at the SACHRP meeting of July 2012.

The FDA's 1998 Information Sheet on local context is out of date and should be archived, but FDA's 2006 guidance on the use of central IRBs ("Using a Centralized IRB Review Process in Multicenter Clinical Trials,") only needs some minor updates.

In the historical context of IRB review in the United States, there traditionally has been great tolerance for local diversity of opinion among local IRBs, which have been encouraged to exercise their freedom to reach decisions based on local circumstances and preferences. Further, by regulation and design, IRBs generally operate as "courts of last resort," as their decisions are most often final and binding.[1] When this system was developed, most research was conducted at a single site, and study designs were individual and unique. In recent years, however, particularly in biomedical research, studies across many sites increasingly share a common study design, having been designed and funded by industry or federal agencies in this way, specifically in order to assure adequate and representative participant enrollment. In a multi-site study, in which sites share a common study design, the risk profile of the study has many more commonalities than differences among the participating sites.

For such studies, the value of local variability ebbs in importance. What become more important, to assure both safety of subjects and scientific value, is that these sites adhere to a common study design and that information about any adverse events/unanticipated problems be analyzed in common and by those with specialized expertise, with findings shared promptly and uniformly across all sites. Because the research environment – at least in these sorts of studies –

[1] Federal authorities of cognizant jurisdiction (e.g., OHRP, FDA, funding agencies) may overturn IRB decisions, but such actions are infrequent and are regarded as exceptional. In addition, in institutions or entities in which research is conducted, the institutions or entities themselves may forbid research from being initiated, even when an IRB has approved the research; but the institutions or entities may not allow research that an IRB has disapproved.

has drastically changed, but because significant differences among sites and local subject populations can remain, SACHRP recommends that FDA and OHRP develop unified guidance that facilitates single IRB review, and assures adequate consideration of true local differences, for studies in which a common study design and unified review will tend to yield better science and greater subject safety. The use of single IRBs can improve quality in these ways, and not just reduce administrative burden, but true local variations in risk must continue to be recognized and accommodated in study design and conduct.

The term "single IRB review" refers to a variety of types of IRBs, with the unifying feature being review of research, regardless of location, by a single IRB. The single IRB can be of several models, such as institution based, independent, central, collaborative, or lead. The term includes IRBs that are the focus of reliance agreements such as Harvard and the Ohio consortium. Central IRBs, such as the NCI and VA central IRBs and independent IRBs, are a subset of single IRBs.

SACHRP recommends that OHRP and FDA issue guidance or FAQs or use another mechanism that harmonizes the use of single IRB review. Such guidance should be applicable to any type of IRB that is at a different location from the research site. To accomplish this goal, SACHRP recommends that FDA make minor modifications to its 2006 guidance on central IRB review. SACHRP also recommends that OHRP issue guidance, by the most practical means, which mirrors as closely as possible the revised 2006 FDA guidance on central IRB review.

The minor revisions to the 2006 FDA guidance should be the removal of footnote 12, which references the archived OHRP guidance, and footnote 13, which references out of date FWA information. The FDA should also harmonize more closely the current sections V and VI so that there is similar guidance for institutions with and without internal IRBs, and less emphasis on the concept of facilitated review introduced by the NCI Central IRB. Finally, SACHRP recommends that FDA add a footnote noting that "central IRBs" are a subset of "single IRBs," and that single IRB review of research should be encouraged for multi-site research and other such situations as well.

After FDA makes these minor changes to the 2006 guidance, OHRP should by the most practical means issue corresponding guidance.
Consistent with 45 CFR 46 (the HHS regulations), FDA regulations, and the FDA 2006 guidance, "the IRB shall be able to ascertain the acceptability of proposed research in terms of institutional commitments and regulations, applicable law, and standards of professional conduct and practice." The revised guidance documents should address, but not be limited to, four key topics that are important for all IRBs : applicable law and local standards , knowledge of institutional policies and capacity, investigator and study staff qualifications, and community and subject considerations.[2] In contrast to prior guidance, the guidance should describe what the IRB must consider rather than dictate procedural requirements.. Often the relevant information can be obtained through the application process and the standard IRB procedures. However, it is important for the IRB to have written procedures and to be prepared to obtain additional information when appropriate, such as through consultation with other parties. IRBs should have

[2] This applies to equally to local IRBs that approve research at the same site where the research is conducted, but the focus of this document is review by IRBs located at a different site from where the research is conducted.

flexibility to obtain this information in the most efficient manner, and given the pace of technological change it is not effective for guidance to recommend specific administrative measures.

Applicable Law and Local Standards

Both HHS and FDA regulations require that "the IRB shall be able to ascertain the acceptability of proposed research in terms of institutional commitments and regulations, applicable law, and standards of professional conduct and practice." For any IRB review, including single IRB review of research at an external site(s), the IRB should have access to and consider state and other applicable law.

It would be valuable to IRBs to have access to a public state law data base. SACHRP encourages the development of such a data base.

Knowledge of Institutional Policies and Capacity

As noted above, HHS and FDA regulations require that, among other considerations, "the IRB shall be able to ascertain the acceptability of proposed research in terms of institutional commitments...." For any IRB review, the IRB should have access to and consider institutional capacity, commitments and policies. Institutional capacity includes the resources to support the research such as space, equipment, and personnel. Institutional commitments include policies on issues such as birth control, compensation for injury, or contacts for research subjects' questions.

Investigator and Study Staff Capability

The investigator and study staff should be appropriately qualified to conduct the research through knowledge and experience. When an IRB is reviewing research external to itself, additional efforts may be required to assess the investigator and study staff. The IRB should either assess investigators and study staff itself, or rely upon alternative measures such as an institutional credentialing/privileging process. The IRB should also have access to information about prior research non-compliance, criminal activities, state board issues, etc. Other factors to be considered in assessing qualifications include financial conflicts of interest, research workload, and training in research ethics and the conduct of research.

Community and Subject Considerations

The IRB should have access to information about the prospective subject population. Often some or all of this information will be in the protocol or the IRB application materials. Other times the IRB will need supplemental information such as census data, including race/ethnicity, primary languages, and religious affiliations.

The IRB will need to also have procedures that address extra steps taken for research involving unique cultures and sensitive areas of inquiry, particularly when reviewing non-local research.

SACHRP believes that these changes to guidance will help to increase reliance on single IRB review, which in turn will promote quality and efficiency in human subject protections.